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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,476	09/23/2003	Abraham Shahar	85189-498	4834

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EXAMINER	
NAFF, DAVID M	
ART UNIT	PAPER NUMBER
1657	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/669,476	SHAHAR ET AL	
	Examiner	Art Unit	
	David M. Naff	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-20,23-34 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-20,23-34 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/30/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

An amendment of 10/30/06, in response to an office action of 6/19/06, amended the specification and claims 1, 3, 7, 9, 10, 12-14, 16-20, 23, 25, 26, 28 and 30-34, added new claim 36, and canceled claims 2, 21, 22 and 35.

Claims examined on the merits are 1, 3-20, 23-34 and 36, which are all claims in the application.

Receipt is acknowledged of the drawing (Fig. 2) filed 10/30/06.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1, 4-6, 8, 9, 23, 24, 28, 30 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balazs et al (5,128,326) in view of Skubitz et al (5,703,205) and Zecchino et al (6,497,887 B1).

The claims are drawn to a biocompatible matrix comprising hyaluronic acid and laminin in a ratio of hyaluronic acid to laminin of about 20:1 to about 400:1, and a bioactive compound or drug selected from a group including ascorbic acid and DHEA.

Balazs et al disclose a drug delivery system containing a cross-linked gel formed by cross-linking hyaluronic acid and a polymer together. The polymer can be a glycol protein (col 2, lines 19-23 and 45-49, and col 4, lines 26 and 58-62), and the gel can contain a drug to be delivered. The cross-linked gel can be used in combination with supports or substates (col 4, lines 54-57).

Skubitz et al disclose that laminin is a glycoprotein that occurs in basement membranes (col 1, lines 29-36). Laminin has various functions relating to cells (col 1, line 63 to col 2, line 24, and col 12, lines 4-38). A laminin polypeptide can promote wound healing (col 12, lines 4-7).

Zecchino et al disclose a membrane delivery system containing a biologically active agent for delivery. The agent can be ascorbic acid (col 5, line 41), or a hormone such as estrogen, progesterone or DHEA (col 5, lines 50-55). Other therapeutic agents can be also delivered (paragraph bridging cols 5 and 6).

It would have been obvious to use laminin as the glycoprotein of Balazs et al that is cross-linked with hyaluronic acid as suggested by Skubitz et al disclosing that laminin is a glycoprotein and can have various functions including promoting wound healing that would have been expected to be advantageous when the delivery system of Balazs et al is used to delivery a drug to a wound. A ratio in the range as claimed would have been obvious from Balazs et al disclosing using a solution containing 0.05-2% hyaluronic acid (col 6, lines 55-57) and the cross-linked hyaluronan with a hydrophilic polymer containing 5-95% of insoluble hyaluronan (col 16, lines 36-38) since this will be a ratio of about 20:1 due to the hydrophilic polymer being less than 5% due to the presence of cross-linking agent. It would have been further obvious to use ascorbic acid or DHEA as the drug of Balazs et al to obtain their function as suggested by Zecchino et al disclosing a membrane delivery system for delivery of an active agent that can be

ascorbic acid or DHEA. The viscosity of claim 4, and percentages of hyaluronic acid and laminin of claims 5 and 6 would have been matters of individual preference within the skill of the art. A structural component as in claims 9 and 36 would have been suggested by Balazs et al disclosing using the cross-linked gel in combination with a support or substrate (col 4, lines 54-47). The method for preparing the matrix of claim 23 would have been obvious from the method disclosed by Balazs et al for preparing a cross-linked gel containing a glycoprotein and hyaluronic acid.

Response to Arguments

The amendment urges that there is no motivation to combine Balazs et al with Skubitz et al. However, the motivation is due to Balazs et al disclosing a glycoprotein and Skubitz et al disclosing laminin as a glycoprotein having advantageous properties. A property of laminin is for wound healing that would be expected to be beneficial with the drug delivery system of Balazs et al that can deliver a drug to a wound.

Balazs et al is not limited to the a ratio of 1:1 as in Example 8 since the amount of hyaluronic acid can be 0.05-2% hyaluronic acid in solution, and the hyaluronan cross-linked with a hydrophilic polymer can contain 5-95% of insoluble hyaluronan. This will be a ratio of about 20:1 as claimed. Therefore, 132 declaration filed with the amendment does not obviate the rejection. Moreover, the declaration does not show results when using ratios at lower and upper limits of the ratio range. When using 400:1 and 20:1, the same results may not

be obtained when using 167:1, 67:1 and 33:1, as supported by 1667:1 not giving satisfactory results.

Claim Rejections - 35 USC § 103

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1, 4-6, 8, 9, 23, 24, 28, 30 and 36 above, and further in view of Brodsky et al (4,971,954).

The claim requires a sugar as an exogenous cross-linking agent.

Brodsky et al disclose cross-linking collagen by reacting amino groups of collagen with an aldehyde group of a reducing sugar (col 4, lines 19-60).

When using laminin as the glycoprotein of Balazs et al as set forth above, it would have been obvious to use a reducing sugar as the cross-linking agent of Balazs et al as suggested by Brodsky et al disclosing that the aldehyde group of a reducing sugar reacts with amino groups of collagen to cross-link the collagen since hyaluronic acid contains an amino group that would have been expected to react the reducing sugar in the same type of way as with collagen.

Claim Rejections - 35 USC § 103

Claims 7 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1, 4-6, 8, 9, 23, 24, 28, 30 and 36 above, and further in view of Gao (6,927,204 B2).

The claims require bioactive compounds or drugs including IGF1.

Gao discloses a container containing a pharmaceutically acceptable carrier containing a cell proliferation-inducing amount of IGF1 (col 34, lines 34-40).

When using laminin as the glycoprotein of Balazs et al as set forth above, it would have been obvious to use IGF1 as the drug to be delivered to obtain the function of this drug to induce cell proliferation as disclosed by Gao.

Claim Rejections - 35 USC § 103

Claims 10-20, 25-27 and 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1, 4-6, 8, 9, 23, 24, 28, 30 and 36 above, and further in view of Valentini et al (5,939,323) and Shahar et al (WO 99/58042).

The claims require the matrix to contain cells resulting from cells being cultured in or upon the matrix.

Valentini et al disclose a scaffold formed of hyaluronic acid for use in tissue repair (paragraph bridging cols 1 and 2). The scaffold can contain bioactive agents (col 3, lines 7-19, and col 6, lines 19-49) such as a growth factor (col 6, lines 36-37). Cells can be seeded on the scaffold and grown on the scaffold (col 3, lines 53-62, col 4, lines 3-10, and paragraph bridging cols 7 and 8). Various types of cells can be used depending on the type of tissue repaired, and the cells can be stem cells (col 7, line 42). The scaffold can be a two-phase scaffold by combining a biodegradable polymer such as polylactic acid or polyglycolic acid with the hyaluronic acid (col 3, lines 41-51).

Shahar et al disclose culturing neuronal cells in a matrix gel formed of hyaluronic acid and laminin to form a neuronal implant (paragraph bridging pages 16 and 17, and page 17, line 7, to page 18, line 3).

When using laminin as the glycoprotein of Balazs et al as set forth above, it would have been obvious to culture cells on the gel to provide cells on the gel for implanting as suggested by Valentini et al forming an implant by culturing cells on a hyaluronic acid scaffold and by Shahar et al producing an implant by culturing cells on gel formed of hyaluronic acid and laminin. While Shahar et al culture only neuronal cells, it would have been apparent from Valentini et al that other cells can be cultured on the gel depending on the type of tissue repaired.

Response to Arguments

The amendment argues that the references applied in rejecting the above dependent claims do not overcome the deficiencies of Balazs et al and Skubitz et al. However, for reasons set forth above, Balazs et al and Skubitz et al are still considered to render the invention obvious.

Claim Rejections - 35 USC § 103

Claims 1, 4-6, 9-20, 23-28, 31-34 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valentini et al in view of Balazs et al and Skubitz et al, and if necessary in further view of Shahar et al.

The invention and references are described above.

It would have been obvious a cross-link a glycoprotein and hyaluronic acid together to form the scaffold of Valentini et al as suggested by Balazs et al cross-linking hyaluronic acid and a glycoprotein together, and it would have been obvious to use laminin as the glycoprotein as suggested by Skubitz et al disclosing that laminin is a glycoprotein, and has various functions including enhancing wound healing. Balazs et al would have suggested a ratio in the claimed range. The viscosity of claim 4, and percentages of hyaluronic acid and laminin in claims 5 and 6 would have been matters of individual preference within the skill of the art. A structural component as in claims 9, 19 and 36 would have been suggested by Balazs et al disclosing using the cross-linked gel in combination with a support or substrate (col 4, lines 54-47). The method for preparing the matrix of claim 23 would have been obvious from the method disclosed by Balazs et al for preparing a cross-linked gel containing a glycoprotein and hyaluronic acid. If needed, Shahar et al would have further suggested growing cells on a scaffold formed of hyaluronic acid and laminin.

Response to Arguments

It is granted as urged in the amendment that Valentini et al does not cross-link the hyaluronic acid with laminin. However, such cross-linking would have been obvious when the secondary references are considered. A ratio in the claimed range would have been obvious from Balazs et al for reasons set forth above. The motivation for using

laminin in combination hyaluronic acid is provided by properties of laminin disclosed by Skubitz et al.

Claim Rejections - 35 USC § 103

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1, 4-6, 9-20, 23-28, 31-34 and 36 above, and further in view of Brodsky et al.

The invention and references are described above.

When cross-linking laminin and hyaluronic acid together to form the scaffold of Valentini et al as set forth above, it would have been obvious to use a reducing sugar as a cross-linking agent as suggested by Brodsky et al disclosing that the aldehyde group of a reducing sugar reacts with amino groups of collagen to cross-link the collagen since hyaluronic acid contains an amino group that would have been expected to react with the reducing sugar in the same type of way as with collagen.

Claim Rejections - 35 USC § 103

Claims 7 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1, 4-6, 9-20, 23-28, 31-34 and 36 above, and further in view of Gao.

The invention and references are described above.

When cross-linking laminin and hyaluronic acid together to form the scaffold of Valentini et al containing a bioactive agent as set forth above, it would have been obvious to use IGF1 as the bioactive agent to obtain the function of this agent to induce cell proliferation as disclosed by Gao.

Claim Rejections - 35 USC § 103

Claims 8 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1, 4-6, 9-20, 23-28, 31-34 and 36 above, and further in view of Zecchino et al.

The invention and references are described above.

When cross-linking laminin and hyaluronic acid together to form the scaffold of Valentini et al containing a bioactive agent as set forth above, it would have been obvious to use ascorbic acid or DHEA as the bioactive agent to obtain their function as suggested by Zecchino et al disclosing a membrane delivery system for delivery of an active agent that can be ascorbic acid or DHEA.

Response to Arguments

The amendment argues that the references used in rejection of the above dependents do not obviate deficiencies of Valentini et al, Balazs et al and Skubitz et al. However, for reasons set forth above, Valentini et al, Balazs et al and Skubitz et al are still considered to render the invention obvious.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

David M. Naff
Primary Examiner
Art Unit 1657

DMN
1/16/07